Paper No. 31

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte JONATHAN STAMLER, JOSEPH LOSCALZO,
DANIEL SIMON and DAVID SINGEL

Appeal No. 2000-0894
Application No. 08/437,884

ON BRIEF

Before WINTERS, MILLS, and GRIMES, Administrative Patent Judges.

GRIMES, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 48-66. Claims 48, 55, and 65 are representative and read as follows:

> 48. A method for delivering a charged nitrogen monoxide species to a targeted site in a patient comprising administering to the patient a compound comprising an immunoglobulin molecule bonded to at least one nitrogen monoxide moiety, wherein the immunoglobulin molecule delivers the charged nitrogen monoxide species under physiological conditions at the targeted site in the patient.

55. A compound comprising an immunogkobulin molecule bonded to at least one nitrogen monoxide moiety, wherein the immunoglobulin molecule delivers a charged nitrogen monoxide species under physiological conditions.

65. A method of treating or preventing cardiovascular disorders in a patient comprising administering to the patient the compound of claim 55.

The examiner relies on the following references:

Hawiger et al. (Hawiger)	4,703,039	Oct. 27, 1987
Means et al. (Means)	4,900,719	Feb. 13, 1990
Loscalzo et al. (Loscalzo)	5,025,001	Jun. 18, 1991

Claims 48-66 stand rejected under 35 U.S.C. § 103 as obvious over Means, Hawiger, and Loscalzo.

Claim 65 stands rejected under 35 U.S.C. § 112, first paragraph, as unsupported by an enabling disclosure.

We reverse both rejections.

Background

The specification discloses "S-nitroso-protein compounds and their use as a means to . . . endow the protein with new smooth muscle relaxant and platelet inhibitory properties and to provide targeted delivery of nitric oxide to specific bodily sites." Page 1. One disclosed "embodiment of the invention relates to the S-nitroso-immunoglobulin compounds derived from the nitrosylation of immunoglobulins." Id., page 19.

S-nitroso-immunoglobulin compounds are disclosed to "exert vasodilatory and platelet inhibitory effect. Thus, these compounds may be administered as therapeutic agents, to an animal, to promote vasodilation and platelet inhibition,

and to treat or prevent cardiovascular disorders. The half lives of these compounds, in [sic] the order of one day, produce unique, long-lasting vasodilatory effects." Id. The specification includes working examples showing that S-nitroso-immunoglobulin compounds inhibit platelet aggregation and induce relaxation of smooth muscle. See page 50.

Discussion

1. The obviousness rejection

The examiner rejected all of the claims under 35 U.S.C. § 103, as obvious in view of the prior art patents of Means, Hawiger, and Loscalzo. The examiner characterizes Means as teaching "use of nitric oxide moieties conjugated to proteins and/or albumin as a means of increasing the bioavailability of the nitric oxide." Examiner's Answer, page 3. The examiner cites Hawiger as teaching "that carrier molecules such as albumin or immunoglobulin may be used to increase the biological half-life of small molecules (i.e., make the molecules longer acting . . .)." Id., pages 3-4. The examiner cites Loscalzo as teaching that "NO was useful for the inhibition of platelet aggregation and vasodilation and cardiovascular disorders." Id., page 4. He concludes that

> [o]ne of ordinary skill in the art at the time the invention was made would have been motivated to conjugate nitric oxide to immunoglobulins because the resulting immunoconjugate would increase the plasma half-life of the nitric oxide moiety thereby increasing its therapeutic efficacy. . . . From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole is [sic, would have been] prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Id.

> Appellants argue that
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> > the Examiner picked one reference that taught S-nitroso serum albumin (i.e., Means), then picked one reference that taught a peptide-serum albumin conjugate (i.e., Hawiger) and then picked one reference that taught S-nitroso derivatives of ACE inhibitors (i.e., Loscalzo), and then put the references together and asserted that the combination rendered the present claims obvious. The combination of references, however, does not produce the presently claimed invention and does not provide any motivation to arrive at the presently claimed invention.

Appeal Brief, page 9. Appellants also argue that the claimed method provides unexpectedly superior results compared to prior art methods. See id., pages 7-8.

"In proceedings before the Patent and Trademark Office, the Examiner bears the burden of establishing a prima facie case of obviousness based upon the prior art. '[The Examiner] can satisfy this burden only by showing some objective teaching in the prior art or that knowledge generally available to one of ordinary skill in the art would lead that individual to combine the relevant teachings of the references.'" In re Fritch, 972 F.2d 1260, 1265, 23 USPQ2d 1780, 1783 (Fed. Cir. 1992) (citations omitted). An adequate showing of motivation to combine requires "evidence that 'a skilled artisan, confronted with the same problems as the inventor and with no knowledge of the claimed invention, would select the elements from the cited prior art references for combination in the manner claimed.'" Ecolochem, Inc. v. Southern Calif. Edison Co., 227 F.3d 1361, 1375, 56 USPQ2d 1065, 1075 (Fed. Cir. 2000) (quoting In re Rouffet, 149 F.3d 1350, 1357, 47 USPQ2d 1453, 1456 (Fed. Cir. 1998)).

We agree with Appellants that the examiner has not met his burden of showing prima facie obviousness. The examiner argues that Hawiger teaches "that carrier molecules such as albumin or immunoglobulin may be used to increase the biological half-life of small molecules (i.e., make the molecules longer acting," Examiner's Answer, pages 3-4, and therefore "[o]ne of ordinary skill in the art at the time the invention was made would have been motivated to conjugate nitric oxide to immunoglobulins because the resulting immuno-conjugate would increase the plasma half-life of the nitric oxide moiety thereby increasing its therapeutic efficacy. Id., page 4.

The examiner's characterization of Hawiger, however, seriously overstates its relevance to the instant claims. Although the examiner characterizes Hawiger as teaching "that carrier molecules such as albumin or immunoglobulin may be used to increase the biological half-life of small molecules," the disclosure of Hawiger is limited to conjugating peptides to a carrier protein such as albumin or immunoglobulin. See, e.g., column 1, lines 19-25 ("The present invention relates to . . . peptide conjugates."); column 2, lines 66-67 ("The conjugate is formed of one or more peptides and a carrier molecule selected from the group consisting of proteins . . ."); and column 3, lines 25-26 ("The carrier molecule is preferably selected from a group consisting of . . . immunoglobulin."). The examiner's attempt to broaden Hawiger's teaching from the disclosed peptide/protein conjugates to NO/protein conjugates is without evidentiary support. Therefore, Hawiger cannot be relied on to supply the requisite motivation to combine the cited references.

The examiner has pointed to nothing in the remaining references that would have led those skilled in the art to make the required combination. We have reviewed the cited references but we find nothing in them that would have suggested the claimed invention to those of ordinary skill in the art. Means teaches protein/NO conjugates that provide the same therapeutic effect as the known antihypertensive drug sodium nitroprusside (SNP), but in a form that does not result in toxic degradation products that limit the use of SNP. See column 1, line 65 to column 2, line 33. The proteins in Means' protein/NO conjugates are glutathione and serum albumin. See column 1, lines 1-15. Loscalzo teaches S-nitrosothiol derivatives of ACE (angiotensin converting enzyme) inhibitors, but the ACE inhibitors are relatively small chemical compounds, not peptides or proteins. The examiner has not adequately explained how Means or Loscalzo would have motivated a person of ordinary skill in the art to conjugate NO to an immunoglobulin.

Thus, we conclude that the cited references, do not provide the requisite motivation to combine a nitrogen monoxide moiety with an immunoglobulin. "Combining prior art references without evidence of such a suggestion, teaching, or motivation simply takes the inventor's disclosure as a blueprint for piecing together the prior art to defeat patentability—the essence of hindsight." In re Dembiczak, 175 F.3d 994, 999, 50 USPQ2d 1614, 1617 (Fed. Cir. 1999) (citations omitted).

Since we conclude that the references do not support a prima facie case under 35 U.S.C. § 103, we need not address Appellants' evidence of unexpected results.

2. The nonenablement rejection

The examiner rejected claim 65 under 35 U.S.C. § 112, first paragraph, "because the specification, while being enabling for a method of treating cardiovascular disorders with NO immunoglobulins, does not reasonably provide enablement for preventing cardiovascular disorders with NO immunoglobulins." Examiner's Answer, page 4 (emphasis added). The examiner explains that "[t]he specification fails to enable the 'prevention' of cardiovascular disorders. . . . Prevention has been viewed as requiring the absolute and complete elimination of any cardiovascular disorders and the specification fails to enable a claim of that nature." Id., page 5.

We begin our analysis with the examiner's claim construction. See In re Moore, 439 F.2d 1232, 1235, 169 USPQ 236, 238 (CCPA 1971) ("[W]hen the first paragraph [of 35 U.S.C. § 112] speaks of 'the invention,' it can only be referring to that invention which the applicant wishes to have protected by the patent grant, i.e., the claimed invention. For this reason the claims must be analyzed first in order to determine exactly what subject matter they encompass."). When construing claims during prosecution, "the PTO applies to the verbiage of the proposed claims the broadest reasonable meaning of the words in their ordinary usage as they would be understood by one of ordinary skill in the art, taking into account whatever enlightenment by way of definitions

or otherwise that may be afforded by the written description contained in the applicant's specification." In re Morris, 127 F.3d 1048, 1054, 44 USPQ2d 1023, 1027 (Fed. Cir. 1997).

The examiner construed the claimed "method of . . . preventing cardiovascular disorders" to "requir[e] the absolute and complete elimination of any cardiovascular disorders." Examiner's Answer, page 5. Appellants argue that this construction is "improper and not supported by any rule or law." Appeal Brief, pages 12-13.

We agree with Appellants that the examiner erred in construing the claim language. The examiner's interpretation of prevention to require "absolute and complete" prevention is unreasonable. The examiner has cited no dictionary definition, scientific treatise, or case law as the basis for interpreting a "method of preventing" disease to require "absolute and complete" prevention of the disease.

Claim language must be interpreted in light of the specification. See In re Sneed, 710 F.2d 1544,1548, 218 USPQ 385, 388 (Fed. Cir. 1983) ("[C]laim language should be read in light of the specification as it would be interpreted by one of ordinary skill in the art."). Here, the specification states that "S-nitroso-immunoglobulin compounds derived from the nitrosylation of immunoglobulins . . . exert vasodilatory and platelet inhibitory effect. Thus, these compounds may be administered as therapeutic agents, to an animal, to promote vasodilation and platelet inhibition, and to treat or prevent cardiovascular disorders." Page 19. Thus, read in light of the specification, the claimed "method of . . . preventing cardiovascular disorders" is properly interpreted to mean that the claimed method

causes vasodilation and inhibition of platelet aggregation, thereby preventing cardiovascular disorders. That is, the claimed method results in vasodilation and inhibition of platelet aggregation, and these effects reduce the risk of, i.e., "prevent," cardiovascular disorders.

The specification provides evidence that the claimed method results in vasodilation and inhibition of platelet aggregation. See page 50. The examiner has presented no evidence to the contrary. Therefore, the rejection for nonenablement is not supported by a preponderance of the evidence. The rejection is reversed.

Summary

We reverse the rejection under 35 U.S.C. § 103 because the references cited by the examiner provide no motivation to combine the elements of the claimed invention. We reverse the rejection for nonenablement because it is based on an erroneous interpretation of the claim language.

REVERSED

SHERMAN D. WINTERS Administrative Patent Judge	)
	) BOARD OF PATENT
DEMETRA J. MILLS Administrative Patent Judge	) APPEALS AND
	) INTERFERENCES
ERIC GRIMES Administrative Patent Judge	)

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